

REMARKS

Claims 1-5, 8, 15-20, and 37-40 constitute the pending claims in this application. Applicants have amended claims 1 and 15 to clarify the subject matter. Support for the amendment can be found throughout the specification (*e.g.*, page 2, lines 15-26; page 8, lines 9-22; Figures 1-4). No new matter has been added.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Rejection of Claims 1-5, 8, 15-20, and 39-40 under 35 U.S.C. § 102(a)

Claims 1-5, 8, 15-20, and 39-40 are rejected under 35 U.S.C. § 102(a) as being allegedly anticipated by Alizadeh *et al.* (*Nature* (February 2000) 403:503-511), referred to herein as Alizadeh *et al.* (2000).

Applicants have amended claims 1 and 15 to more particularly define the term “informative gene.” The amendments are fully supported by the specification. For example, the specification teaches that “[g]enes that are particularly relevant for classification have been identified as a result of work described herein and are shown in Figures 1, 2A, 2B, 3A, 3B, 4A and 4B. The genes that are relevant for classification are referred to herein as ‘informative genes’” (*see, e.g.*, page 8, lines 9-22).

Applicants submit that the claim amendments meet the requirements as set forth in M.P.E.P. 2173.05(s), which provides that incorporation by reference to a specific figure or table is permitted “where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim.”

Applicants submit that the pending claims, as amended, are novel over Alizadeh *et al.* (2000) because Alizadeh *et al.* (2000) neither teach nor suggest all the elements of the claimed invention.

Claim 1 as amended is directed to a method of classifying a lymphoma sample according to predicted treatment outcome comprising determining a gene expression profile of gene expression products from two or more informative genes selected from the group consisting of

the genes in Figures 1, 2A, and 2B excluding the p16 gene, wherein the gene expression products are isolated from one or more cells in the sample, wherein the gene expression profile is correlated with a treatment outcome, thereby classifying the sample with respect to treatment outcome.

Claim 15 as amended is directed to a method of classifying a sample according to lymphoma type comprising determining a gene expression profile of gene expression products from two or more informative genes selected from the group consisting of the genes in Figures 3A, 3B, 4A, and 4B excluding the cathepsin B gene, the cyclin B1 gene, and the CD3 epsilon gene, wherein the gene expression product is isolated from one or more cells in the sample, wherein the gene expression profile is correlated with a lymphoma type, thereby classifying the sample with respect to lymphoma type.

In contrast, Alizadeh *et al.* (2000) describe a method of subdividing a single lymphoma type (*e.g.*, diffuse large B-cell lymphomas) into distinct subtypes by analyzing differential gene expression signatures (see, *e.g.*, the abstract; Figures 3-4). Alizadeh *et al.* (2000) do not disclose any of the informative genes as recited in amended claim 1 or 15. Nor do Alizadeh *et al.* (2000) disclose a method of classifying a lymphoma sample by determining a gene expression profile of any of these informative genes. Accordingly, Alizadeh *et al.* (2000) fail to teach the method of claim 1 or 15.

In sum, Applicants submit that independent claims 1 and 15, as well as claims dependent thereon, are novel and not obvious in view of the teachings of Alizadeh *et al.* (2000) because Alizadeh *et al.* (2000) do not teach or suggest all the elements of the invention of claims 1 or 15. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 1-5, 8, 15-20, and 39-40 under 35 U.S.C. § 102(b)

Claims 1-5, 8, 15-20, and 39-40 are rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Alizadeh *et al.* (Cold Spring Harbor Symposium Quantitative Biology (June 1999) 64:71-78), referred to herein as Alizadeh *et al.* (1999).

As described above, Applicants have amended claims 1 and 15 to more particularly define the term “informative gene.”

Alizadeh *et al.* (1999) merely describe a method of subdividing lymphoma samples of a single lymphoma type (*e.g.*, diffuse large-cell lymphomas) into subtypes by analyzing differential gene expression signatures (see, *e.g.*, Figures 1-2). However, Alizadeh *et al.* (1999) do not teach a method of classifying a lymphoma sample according to predicted treatment outcome as recited in amended claim 1. Although Alizadeh *et al.* (1999) briefly mention that “it may be possible to use gene expression profiles to predict whether a patient is likely to fail to particular treatment regimen” (page 77, column 1), Applicants submit that the teachings of Alizadeh *et al.* (1999) are not enabling. At the time the Alizadeh *et al.* (1999) reference was published, one could merely have hoped that gene expression profiles would predict the treatment outcomes of a patient. In the absence of further guidance or protocols, the Alizadeh *et al.* (1999) reference is merely an invitation to experiment with no expectation of success. Indeed, one skilled in the art would not have known how to practice the method for predicting the treatment outcome proposed by Alizadeh *et al.* (1999). In contrast, the present application not only teaches in detail the method recited in claim 1, but also provides working examples illustrating the effective use of the informative genes listed in Figures 1-2 in predicting treatment outcomes.

Further, Applicants submit that Alizadeh *et al.* (1999) do not disclose any of the informative genes as recited in amended claim 1 or 15. Nor do Alizadeh *et al.* (1999) disclose a method of classifying a lymphoma sample by determining a gene expression profile of any of these informative genes. Accordingly, Alizadeh *et al.* (1999) fail to teach the method of claim 1 or 15.

In sum, Applicants submit that independent claims 1 and 15, as well as claims dependent thereon, are novel and not obvious in view of the teachings of Alizadeh *et al.* (1999) because Alizadeh *et al.* (1999) do not teach or suggest all the elements of the invention of claims 1 or 15. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 1-5, 8, 15-20, and 37-40 under 35 U.S.C. § 102(e)

Claims 1-5, 8, 15-20, and 37-40 are rejected under 35 U.S.C. § 102(e) as being allegedly anticipated by Golub *et al.* (U.S. Patent No. 6,647,341). Specifically, the Examiner asserts that

the rejection is maintained because the Declaration under 37 CFR § 1.132 filed on January 10, 2005 was not signed.

Applicants respectfully submit that an executed copy of the Declaration of Dr. Pablo Tamayo under 37 CFR § 1.132 was filed on March 2, 2005. A copy of the executed Declaration of Dr. Pablo Tamayo is enclosed herewith. Applicants reiterate the arguments already made of record and contend that this Declaration shows that Dr. Tamayo, Golub, and Lander “conceived or invented the subject matter disclosed in the patent or application publication and relied on in the rejection” (M.P.E.P. 715.01(a)). Applicants submit that this Declaration under 37 CFR § 1.132 provides a satisfactory showing that “the reference discloses subject matter derived from the applicant rather than invented by the author or patentee notwithstanding the authorship of the article or the inventorship of the patent” (M.P.E.P. 716.10). Thus, this Declaration renders the Golub *et al.* reference unavailable as prior art against this application. Consequently, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 102(e) be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945, under Order No. WIBL-P01-579.**

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